Background Microsatellite instability (MSI) tumors are characterized by defects in the DNA mismatch repair (MMR) genes that lead to the accumulation of mutations within microsatellite (MS) loci. Indels in MS regions of coding genes can result in the synthesis of shared frameshift peptide (FSP) neoantigens, expected to be immunogenic and safe. MSI tumors develop sporadically or secondary to hereditary predisposition as part of Lynch Syndrome (LS), one of the most common hereditary colorectal cancers. Nous-209 is a genetic vaccine encoding 209 neoantigens shared across sporadic and hereditary MSI tumors developed for interception and treatment of MSI tumors.¹ A phase I trial (NCT04041310) combining the Nous-209 vaccine with pembrolizumab anti-PD-1 antibody has been recently completed in metastatic colorectal, gastric and gastro-esophageal cancer patients showing excellent safety, immunogenicity is evaluated on PBMC before and after vaccination by ELISpot assay. No immune events (SAEs) were observed (n=10), and the treatment appears safe and well tolerated. Immunogenicity was demonstrated in 100% of tested patients (n=10) with a mean peak IFN-g SFCs/million PBMCs. No immune responses were detected at baseline prior vaccination in either previvors or survivors LS carriers. Nous-209-induced T cell responses were broad, recognizing different FSPs with induction of both CD4 and CD8 T cell responses. Deconvolution of T cell responses against predicted CD8 epitopes included in the FSPs pools showed multiple positive responses, confirming the optimal breadth of immune responses.

Conclusions Nous-209 is safe, well tolerated, and elicits potent and broad immune response in both LS carriers previvors and survivors, supporting Nous-209 development as a compelling approach for LS cancer interception.

REFERENCES

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